



Diabetic foot ulcers: recent advances and future directions

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Diabetic foot ulcers (DFUs) remain a major complication of diabetes, affecting approximately 18.6 million people worldwide each year. As outlined in the comprehensive JAMA review [1] by Tze Woei Tan, Andrew Boulton, Sicco Bus and myself, DFUs lead to high rates of hospitalization, amputation, and death. Several recent advances provide hope for improved prevention and treatment of these debilitating wounds.

Epidemiological studies have further delineated the disproportionate burden of DFUs and amputations among minorities and those of lower socioeconomic status. For example, long-term rates of major amputation were nearly 3-fold higher in Black vs. White Medicare beneficiaries in the United States. Efforts to address such disparities must remain a priority globally.

Pathophysiologically, we now better understand that sensory, motor, and autonomic neuropathy contribute to callus formation and repetitive trauma during walking. These biomechanical factors, along with peripheral artery disease in approximately half of cases, culminate in tissue damage and ulcer formation.

Regarding classification, the validated Wound, Ischemia, and foot Infection (WIFI) system now allows stratification of ulcers based on severity of tissue loss, ischemia, and infection. WIFI scores strongly predict amputation risk and help identify patients requiring urgent revascularization. This represents

a major advance in prognostication and communication between multidisciplinary team members.

In terms of screening, annual foot exams by podiatrists for those at high risk are clearly beneficial. For example, new ulcer rates were 39% lower among those with prior podiatry care. At-home thermometry also shows promise as a simple, low-cost method for preventing recurrence.

For treatment, multidisciplinary teams including podiatrists, infectious disease specialists, and vascular surgeons reduce major amputation rates up to 60% compared to usual care. This underscores the value of a coordinated approach. Offloading with total contact casting is underutilized but highly effective. Flexor tenotomy and Achilles lengthening may benefit select cases with localized plantar ulcers. Topical oxygen, placenta extracts, and advanced dressings can improve healing in some wounds. Revascularization within 2 weeks reduces major amputation risk 3-fold, highlighting the importance of timely referral.

In summary, we have made strides in DFU epidemiology, classification, screening, multidisciplinary care, and advanced therapeutics. However, challenges remain in preventing initial and recurrent ulcers and overcoming disparities. Ongoing research into genetic, microbial, and immunologic factors may uncover new directions. Refining technologies such as smart socks with embedded sensors, intelligent offloading devices, wound imaging with artificial intelligence, and regenerative medicine approaches

could transform care. While much progress has been made, the ultimate goal is preventing these disabling and deadly wounds in the first place.

Looking ahead, emerging research suggests that alterations in the microbiome and cutaneous immune dysfunction may contribute to delayed healing in some DFUs. Characterizing the microbial ecology and immunologic profile of recalcitrant ulcers could lead to more targeted therapeutic approaches. Additionally, progress continues in regenerative medicine using stem cells and tissue-engineered skin constructs to restore the complex structure and function of damaged skin. Early studies showing improved healing with allogeneic adipose-derived stem cells and bilayered bioengineered skin substitutes represent exciting steps forward.

As highlighted in our JAMA review, a paradigm shift toward personalized, precision care for DFUs

is needed. Rather than a one-size-fits-all protocol, understanding each patient's distinct biomechanical, vascular, microbial, and immunologic profile promises individually tailored treatments [1]. Collaborations between podiatry, infectious disease, vascular surgery, immunology, microbiology, genetics, and regenerative medicine will accelerate the progress in this field. The potential to prevent limb loss and save lives is immense.

Disclosure

The author declares no conflict of interest.

References

1. Armstrong DG, Tan TW, Boulton AJM, Bus SA. Diabetic foot ulcers: A review. *JAMA* 2023; 330: 62–75. DOI: 10.1001/jama.2023.10578